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Certifier D. Hawkins

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2002D–0237]

International Conference on Harmonisation; Evaluation of Stability Data; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance entitled "Q1E Evaluation of Stability Data." The guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This guidance is a supplement to an ICH guidance entitled "Q1A(R2) Stability Testing of New Drug Substances and Products," which was revised from Q1A(R) and published in the **Federal Register** of November 21, 2003 (68 FR 65717). It is intended to provide guidance on how to use stability data, generated in accordance with the principles outlined in Q1A(R2), to propose a retest period for the drug substance and a shelf life for the drug product.

DATES: The guidance is effective [*insert date of publication in the* **Federal Register**]. Submit written or electronic comments at any time.

ADDRESSES: Submit written comments on the guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. Submit written requests for single copies of

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the guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or the Office of Communication, Training, and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–3844. Send two self-addressed adhesive labels to assist the office in processing your requests. Requests and comments should be identified with the docket number found in brackets in the heading of this document. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance: Chi-wan Chen, Center for Drug Evaluation and Research (HFD–830), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2001; or Andrew Shrake, Center for Biologics Evaluation and Research (HFM–345), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1148, 301–402–4635.

Regarding the ICH: Janet Showalter, Office of International Programs (HFG–1), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–0864.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking

scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission, the European Federation of Pharmaceutical Industries Associations, the Japanese Ministry of Health, Labour, and Welfare, the Japanese Pharmaceutical Manufacturers Association, the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA, and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, Health Canada's Health Products and Food Branch, and the European Free Trade Area.

In the **Federal Register** of June 14, 2002 (67 FR 40949), FDA published a draft tripartite guidance entitled "Evaluation of Stability Data." The notice gave interested persons an opportunity to submit comments by August 1, 2002.

After consideration of the comments received and revisions to the guidance, a final draft of the guidance was submitted to the ICH Steering Committee and endorsed by the three participating regulatory agencies in February 2003.

This guidance complements an ICH guidance entitled "Q1A(R2) Stability Testing of New Drug Substances and Products," which was revised from Q1A(R) and published in the **Federal Register** of November 21, 2003. The guidance is intended to provide recommendations on how to use stability data, generated in accordance with the principles outlined in Q1A(R2), to propose a retest period for the drug substance and a shelf life for the drug product.

The recommendations on the evaluation and statistical analysis of stability data provided in Q1A(R2) are brief in nature and limited in scope. Although Q1A(R2) states that regression analysis is an acceptable approach to analyzing quantitative stability data for retest period or shelf life estimation and recommends that a statistical test for batch poolability be performed using a level of significance of 0.25, it includes few details. In addition, Q1A(R2) does not cover situations where multiple factors are involved in a full- or reduced-design study. This guidance provides a clear explanation of the expectations when proposing a retest period or shelf life and storage conditions based on the evaluation of stability data for both quantitative and qualitative test attributes. It outlines recommendations for establishing a retest period or shelf life based on stability data from single or multifactor and full- or reduced-design studies. The guidance further describes when and how limited extrapolation can be undertaken to propose a retest period or shelf life beyond the observed range of data from the long-term storage condition.

This guidance represents the agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the guidance. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at *http://www.fda.gov/ohrms/dockets/default.htm, http://www.fda.gov/cder/guidance/index.htm*, or *http://www.fda.gov/cber/publications.htm*.

Dated: 5/29/04

May 29, 2004.

Jeffrey Shuren,
Assistant Commissioner for Policy.

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